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The role of computed tomography hounsfield unit values in the differentiation of benign and malignant cavitary lung lesions

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Abstract
Aim: This study aims to investigate the role of Hounsfield unit (HU) values measured by contrast-enhanced computed tomography (CT) in the differentiation of benign and malignant cavitary lesions (CLs), which are frequently encountered in the lung parenchyma.
Material and Methods: In this retrospective descriptive study approved by the relevant ethics committee, thoracic CT records taken for various reasons between 2019 and 2021 were scanned from the hospital database. According to the demographic characteristics and histopathological results, the patients were divided into benign and malignant groups. The HU values of 24 patients with CLs were measured by CT and the averages were calculated. HU values were compared by independent t-test.
Results: Of the 24 patients, 20 were male (83.3%) and 4 were female (16.7%), and the mean age was 59.98±16.65 (22-78) years. There were a total of 34 cavitary lung lesions in these 24 patients, including 18 benign (52.94%) and 16 malignant (47.06%) lesions. The mean age of 13 patients (54.17%) with benign etiology was 51.62±18.79 (22-78) and the mean size of all benign lesions was 30.05±9.51 (16-53) mm. The mean age of the 11 patients (45.83%) with malignant etiology was 68.55±6.56 (57-78) and the mean size of all malignant lesions was 39.25±23.45 (13-95) mm. The mean HU values of the 18 benign and 16 malignant CLs were 32.11±12.25 (15-60) and 63.88±24.5 (15-109), respectively, representing a statistically significant difference (p=0.001). In receiver operating characteristic curve analysis, the area under the curve was 86.8%, and when the cut-off was determined as 41.5, the sensitivity was 87.5% and the specificity was 88.9%.
Discussion: We think that HU density values measured from the CL wall by contrast-enhanced CT may be useful in the differentiation of frequently detected benign and malignant CLs, which have similar radiological imaging findings.

Keywords
Computed Tomography, Hounsfield Unit, Cavitary Lung Lesion, Benign, Malignant

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Introduction

Cavitary lesions (CLs) are defined as gas-filled areas that appear radiologically as radiolucent areas or cavities surrounded by well-defined thick walls of various shapes within a pulmonary parenchymal consolidation, mass, or nodule, usually caused by the connection of necrotic lesions throughout the bronchial structures [1]. A wide variety of malignant and benign lesions may present as CLs, including malignancies, infections, autoimmune processes, and congenital diseases [2].

Although there are several specific guidelines [2, 3] published to date on the appropriate approach to CLs, most studies on radiological diagnostic approaches to CLs have been based on chest radiography [4]. Thoracic multidetector computed tomography (CT) is currently the preferred imaging method for evaluating CLs as it provides accurate information about the dimension, shape, and site of CLs and other features that are not evident on radiographs [2, 3]. Considering these data, with accurate clinical and laboratory results, radiologists can narrow the list of possible diagnoses, including benign and malignant pathologies [1-4]. However, limited data are available regarding the objective assessment of CLs by thoracic CT. There are various imaging findings that have been described to distinguish benign and malignant CLs, such as bronchiectasis and accompanying peripheral small airway disease, "halo" and "reverse halo" signs, inner wall irregularity, outer contour features, associated bronchial wall thickening, satellite nodules, consolidation, and accompanying ground-glass opacities [5]. However, since these findings are not specific, there are difficulties in differential diagnosis. As far as we have seen in the literature, there are no published studies that have focused on measuring density in the CL wall of the lung on CT.

In light of the considerable overlap in imaging findings that exists between the various CLs of the lung, it is important to clarify the thoracic imaging findings of CLs that can help in identifying a systematic clinical approach and complications that may require appropriate management. In addition to the imaging clues that have previously been described, our aim in this study is to determine the role of Hounsfield unit (HU) values measured from the CL wall by contrast-enhanced CT in the differentiation of frequently detected benign and malignant CLs, which have similar radiological appearances.

Material and Methods

Study design

This single-center retrospective observational study was initiated with the approval of the medical faculty's clinical research ethics committee with ethical approval number 22.05.2020/150.

In our study, thoracic CT records taken in the radiology clinic for various reasons between January 2019 and January 2021 were retrospectively scanned using the picture archiving and communication systems (PACS) archive of the university hospital. Of the 219 patients who had lung lesions as a result of screening, 148 patients without CLs and 41 patients without pathological results or clinical and radiological follow-up were excluded from the study. In addition, patients with CLs and non-contrast thoracic CT (n=6) were not included in the study because of the retrospective nature of the study and the low number of such patients. The study was conducted with 24 patients with contrast-enhanced thoracic CT with pathological results and/or clinical and radiological follow-up. The histopathological results and clinicoradiological follow-up data of the patients were scanned from electronic medical records and the patients were divided into benign and malignant groups.

CT technique

CT scans were taken with a multidetector CT device (Somatom Emotion 16-slice, CT2012E, Siemens AG, Germany). The imaging protocol was as follows: 3-mm slice thickness, 0.777-mm reconstruction, 0.6-s gantry rotation, 120-kV tube voltage, 200-mA tube current, and field of view of 40-50 cm. For routine contrast-enhanced chest CT imaging, 80 mL of non-ionizing contrast agent, iohexol or iopromide, was injected using an automatic injector (CT 9000 ADV, Liebel-Flarsheim, USA) at a rate of 3 mL/s into the forearm vein. For bolus monitoring, a region of interest (ROI) was identified at the descending aorta at the level of the carina starting at 100 HU and scanning was initiated after 10 s. Scanning was performed at 30-40 s in the

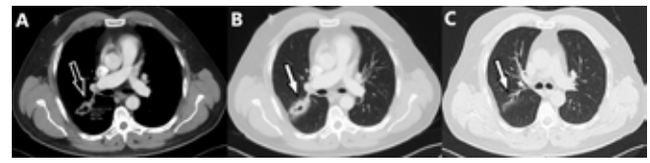

Figure 1. In a 59-year-old male patient, a cavitary lesion, approximately 36 mm in size with lobulated contours and surrounded by ground-glass opacities, is observed on axial sections of the mediastinal (a) and parenchymal (b) windows in the upper lobe of the right lung. The HU value is measured as 39 in the medial wall of the lesion on the mediastinal window (a). The lesion, which is understood to be a pneumonic infiltration in clinical and radiological follow-up, disappears in the control CT scan (c) performed at the 3rd month after treatment.

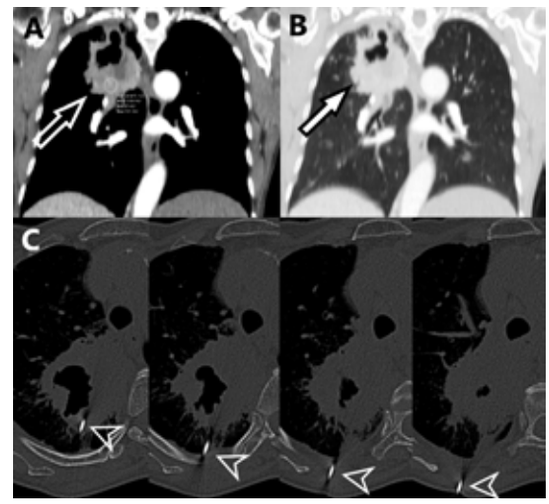

Figure 2. A 62-year-old female patient has a thick-walled cavitary lesion with a spicule contour, approximately 62 mm in size, in the apical region of the right upper lobe of the lung on coronal sections of the mediastinal (a) and parenchymal (b) windows. The HU value is measured as 109 in the inferior wall of the lesion on the mediastinal window (a). The lesion pathology was reported as lung squamous cell carcinoma after CT-guided percutaneous Tru-Cut biopsy (c, arrowheads) performed in the interventional radiology unit.

arterial phase. Sections from the lower cervical to the upper abdominal level were obtained with a contrast agent, with patients in the supine position during CT imaging. An experienced radiologist (7 years) used a high-resolution and grayscale work station in CT evaluations to independently evaluate axial and multiplane reformatted images in mediastinal and parenchymal windows in terms of size, morphology, and CT-HU measurements of CLs. The radiologist had no previous knowledge of the clinical findings or histopathological diagnoses. Numbers and sizes (maximum diameters) of CLs were calculated for each examination on contrast-enhanced CT. In addition, the HU values were measured from the circular ROI drawn from the place where the thickness and enhancement of the CL wall were the highest, and the results were recorded. The lower limit for the ROI was determined as 32 mm2. When the ROI measurement area was drawn, it was ensured that the ROI was in the central part of the measured wall and did not overflow into the lung parenchyma and the air-containing central part of the adjacent CL (Figures 1 and 2). The averages of the obtained HU values were calculated separately for benign and malignant cases. All malignant lesions had a histopathological diagnosis. Among the benign cases, there was a histopathological diagnosis of tuberculosis in 4 cases and rheumatoid nodule in 1 case, while the diagnosis of other benign pathologies was decided according to the clinical approach and the response of the lesions to treatment or spontaneous regression after radiological follow-up.

Statistical Analysis

Descriptive statistics for the continuous variables of the study were expressed as mean, standard deviation (SD), minimum, and maximum and categorical variables as numbers and percentages. Independent 2-sample t-tests were used to compare mean values of benign and malignant cavitary lung lesions in terms of HU values. The statistical significance level was determined as 0.05 in the calculations and SPSS 21.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Sensitivity and specificity values were calculated and the percentages were obtained. An optimum cut-off value for HU density was determined with receiver operating characteristic (ROC) curve analysis.

Results

Of the 24 patients in our study, 20 were male (83.3%) and 4 were female (16.7%), and the mean age was 59.98±16.65 (22-78) years. There were a total of 34 cavitary lung lesions in 24 patients, with 18 being benign (52.94%) and 16 malignant (52.94%). The average diameter of all lesions was 34.62±17.78 (13-95) mm and 16 of the lesions were detected in the right upper lobe (47.06%), 8 were in the left lower lobe (23.53%), 7 were in the right lower lobe (20.59%), and 3 were in the left upper lobe (8.82%). While benign lesions showed a balanced distribution in the lung lobes, malignant lesions were mostly detected in the right upper lobe. In addition, all lesions detected in the left upper lobe were benign (Table 1).

In a total of 13 patients (54.17%) with benign etiology, there were 6 cases of pneumonic infiltrations (46.16%) (Figure 1), 4 cases of tuberculosis (30.77%), 1 case of rheumatoid nodule (7.69%), 1 case of necrotizing pneumonia (7.69%) and 1 case of pulmonary embolism (7.69%). The mean age of patients with benign etiology was 51.62±18.79 (22-78) years and the mean size of all benign lesions was 30.05±9.51 (16-53) mm. There were 6 CLs in 1 patient with a diagnosis of rheumatoid arthritis. In a total of 11 patients (45.83%) with malignant etiology, there were 5 case of squamous cell carcinoma (SCC) (45.45%) (Figure 2), 3 cases of metastases (27.27%) (2 rectal, 1 lung adenocarcinoma), 1 case of primary lung adenocarcinoma (9.09%), 1 case of small cell neuroendocrine carcinoma (9.09%),

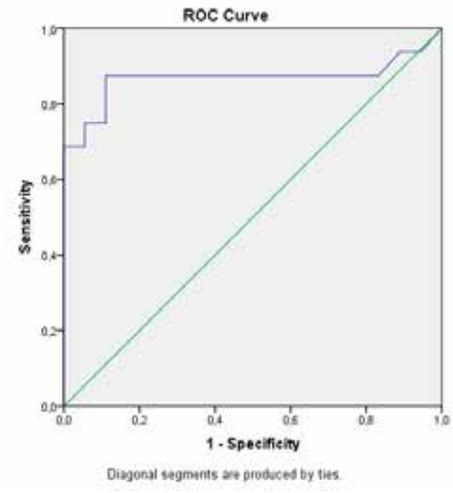

Figure 3. In receiver operating characteristic (ROC) curve analysis (area under the curve: 0.868), when the cut-off HU value was determined as 41.5, the sensitivity for malignant etiologies was 87.5% and the specificity was 88.9%.

Table 1. Comparable clinical variables between malignant and benign cavitary lung lesions

Variable	Malignant (11 patients, 16 lesions)			Benign (13 patients, 18 lesions)			Total (24 patients, 34 lesions)		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
Age	68.55	±6.56	57-78	51.62	±18.79	22-78	59.98	±16.65	22-78
Size (mm)	39.25	±23.45	13-95	30.05	±9.51	16-53	34.62	±17.78	13-95
Hounsfield units	63.88	±24.5	15-109	32.11	±12.25	15-60	47.06	±24.68	15-109
Gender (n=24)	No.		%	No.		%	No.		%
Male	9		81.8	11		84.6	20		83.3
Female	2		18.2	2		15.4	4		16.7
Lesion locations (n=34)	No.		%	No.		%	No.		%
Right upper lobe	11		32.35	5		14.71	16		47.06
Right lower lobe	2		5.88	5		14.71	7		20.59
Left upper lobe	-		-	3		8.82	3		8.82
Left lower lobe	3		8.82	5		14.71	8		23.53

and 1 case of unclassified non-small cell lung carcinoma (NSCLC) (9.09%). The mean age of the patients with malignant etiology was 68.55±6.56 (57-78) years and the mean size of all malignant lesions was 39.25±23.45 (13-95) mm. The 2 patients with rectal adenocarcinoma had a total of 7 metastatic cavitary lung lesions (3 in one and 4 in the other).

Mean HU values measured from the wall of 18 benign and 16 malignant cavitary lung lesions by contrast-enhanced thoracic CT were calculated as 32.11±12.25 (15-60) and 63.88±24.5 (15-109), respectively. In G*power (version 3.1.9.4), post hoc analysis of the differences between two independent means (two groups) revealed an effect of 1.64 with mean and SD values. The calculated power (1-beta) was 0.86 considering type I error (alpha) of 0.001, sample size of 34 (group 1: 18, group 2: 16), and effect size of 1.64. A statistically significant difference was found in the independent t-test performed to differentiate benign and malignant cavitary lung lesions (p=0.001). In ROC analysis, the area under the curve was 86.8%, and when the cut-off value was determined as 41.5, the sensitivity and specificity were 87.5% and 88.9%, respectively (Figure 3).

Discussion

CLs in the lungs are frequently encountered in thorax imaging studies and there are various malignant and benign diseases caused by many acquired or congenital pathologies in the differential diagnoses [6, 7]. In the formation of CLs, there are various pathologic processes, such as central necrosis due to insufficient local blood flow, infarction due to obstruction of regional nutrient vascular structures, and obstruction of the bronchus resulting in distal necrosis. Several studies have suggested that primary lung abscess, malignant neoplasm, and secondary tuberculosis are among the most common pathologies underlying CLs in the lungs, followed by metastatic tumors, fungal infections, lymphoma, and vasculitic processes [8, 9]. Malignant conditions and infections are the two main causes of CLs of the lung in adults. CLs are relatively common in primary lung malignancies; the incidence increases up to 11% on chest radiography and 22% on CT [5]. Therefore, it is important to make a differential diagnosis of CLs. The most common primary lung cancer with a cavity is NSCLC, and especially SCC (69-81%). Other types of lung cancers, including adenocarcinomas and small cell carcinomas, are less likely to present with CLs [10]. In our study, among the benign pathologies, the most common cause was pneumonic infection (n=6), followed by post-primary tuberculosis (n=4). Among malignant pathologies, the most common cause was SCC (n=5), followed by metastases (2 rectal, 1 lung adenocarcinoma). Our findings were similar to those available in the literature. Cavitations in metastatic lesions are not as common as in primary lung malignancies, but metastatic CLs have been reported mostly from squamous cell primaries of organs such as the lungs, colon, stomach, head and neck, bladder, and kidneys [9, 11]. In contrast to the literature, all of the cases of cavitary metastases in our study were adenocarcinoma metastases.

Conventional chest radiography and CT are the most commonly used imaging methods to evaluate lung diseases. Although ultrasonography is useful in the evaluation of pleural pathologies such as effusion or mass, it is not useful to evaluate parenchymal pathologies due to reverberation artifacts caused by the high air content of the lungs [12]. Despite recent advances, evaluation of the lungs by magnetic resonance imaging is still very limited due to low spatial resolution, high sensitivity, and motion artifacts [13, 14]. Although positron emission tomography is another widely used method to detect or characterize lesions larger than 8 mm, it lacks specificity in distinguishing between inflammatory and neoplastic lesions [15]. CT still continues to be the best and most sensitive method among all imaging modalities. We therefore planned our study with patients with contrast-enhanced CT scans.

Localization can be helpful in the differential diagnosis of CLs, as some disease processes have a preference for certain regions of the lung. For example, CLs due to post-primary tuberculosis are mainly located in the apical posterior segments of the upper lobes [16], while lung abscesses due to aspiration generally tend to occur in the posterior segment of the upper lobes or the upper segment of the lower lobes [17]. In addition, there is generally upper lobe predominance in CLs of the lungs [5]. Of the tuberculosis cases (n=4) in our study, 2 were in the left upper lobe, 1 in the left lower lobe, and 1 in the right lower lobe. In this study, similar to the literature, while upper lobe predominance (55.88%) was present, all CLs were mostly located in the right upper lobe (47.06%). In addition, while the majority of lesions in the right upper lobe (n=16) in our study were malignant lesions (n=11, 68.75%), all lesions in the left upper lobe were benign. Our study showed that the malignancy potential is higher if a CL is located in the upper lobes of the lung, especially on the right side.

In some disease processes, more than one cavity is formed in the lung, while a single cavity is observed in others. While bronchogenic carcinoma and pyogenic abscess are among the differential diagnoses of a single CL in the lung, metastases, tuberculosis, septic embolism, aspergillosis, and autoimmune diseases often cause multiple CLs [18]. In our study, among the patients with malignant etiology, 2 patients with rectal adenocarcinoma had a total of 7 CLs, 3 in one case and 4 in the other; other malignant etiologies had a single CL. Among the patients with benign etiologies in our study, 1 patient with a diagnosis of rheumatoid arthritis had a total of 6 cavitary rheumatoid lesions; others had a single CL. Similar to the literature, our study showed that both benign and malignant cavitary lesions may be multiple.

Different clinical and radiological parameters may be helpful in evaluating lung CLs, such as the duration of symptoms, internal contour features, and location of the lesions. Clinical findings may help narrow the differential diagnosis of pulmonary CLs. Acute onset symptoms with fever and productive cough suggest an infection, while chronic cough and weight loss together with fatigue suggest malignancy or tuberculosis. The patient's immune status is another factor to consider in determining the cause of cavitation. The radiological approach to a cavitary lung lesion includes the analysis of wall features, intracavitary material, arterial enhancing foci, its relationship with the pleura, environmental changes, and ancillary findings. However, since the specificity of these definitions is low between malignant and benign etiologies, considerable overlap occurs in these clinical and imaging findings [19]. In this study, we have investigated

the role of CT-HU density values measured from the CL wall. In the literature, there is no similar study done with CT-HU density, and in our current study, we found that HU values were quite significant in differentiating benign and malignant CLs.

Some studies have explained that CLs with thicker walls and irregular internal contours can help diagnose primary or metastatic lung cancer [8, 9, 20]. It has been reported from chest radiographs that most lesions with a maximum wall thickness of >15 mm are malignant, but most of those with a maximum wall thickness of ≤4 mm are benign [4]. Other studies have suggested cut-off values of 15 and 3 mm, respectively [3]. In another similar recent study with CT scanning of 96 patients, the cut-off values for CL wall thickness were determined as 27 and 7 mm [19]. Another study evaluating cavity maximum wall thickness on thoracic CT did not find any difference between malignant and benign pathologies. In the same study, however, it was reported that malignant cavities were more likely to have an irregular inner wall and an indentation in the outer wall compared to benign cavities [10]. Although there are similar studies on CT series of patients with CLs in the lungs [8, 9], these findings are still insufficient and sometimes show inconsistencies. Although most CLs are still diagnosed by additional invasive methods such as percutaneous biopsies, comprehensive CT characterization will provide a safer approach to the patient in cases of suspicious lesions as well as avoiding unnecessary research on benign lesions. In the current study, as a noninvasive method, HU density values were measured from the walls of CLs by contrast-enhanced thoracic CT and were found to be higher in cases of malignant lesions (p=0.001). The results of our study showed the highest predictive value in the differentiation of benign and malignant CLs in the lungs with 87.5% sensitivity and 88.9% diagnostic accuracy when the threshold HU value was determined as 41.5.

The small number of patients in our study can be considered a limitation. However, we know that it takes quite a long time to build a good series of CLs. Our second limitation lies in the lack of inter- and intraobserver variability and our final limitation is that there were some differences in the protocols applied for the contrast phase due to the retrospective nature of the study. However, in our clinic, although the amount and duration of contrast in all contrast-enhanced thoracic CT scans, except for the pulmonary embolism protocol, are partially dependent on the patient, these scans are performed according to a standard as specified in the Material and Methods section.

Conclusion

Contrast-enhanced thorax CT is a valuable imaging method for the characterization of lung CLs. We think that HU density values measured from the CL wall during contrast-enhanced thoracic CT may be useful in the differentiation of frequently detected benign and malignant CLs, which have similar radiological imaging findings. We also think that multicenter and prospective studies are needed to help us develop a more accurate approach to CLs in the lungs.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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